Evaluation of veterinary antimicrobial benchmarking systems at farm-level in Europe: Implications for UK ruminant sector

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ABSTRACT

Background: A number of European countries currently conduct mandatory farm-level benchmarking for antimicrobial usage (AMU). This review describes the systems used, with emphasis on metric type and practical implications.

Methods: This report describes examples of four types of metrics used to measure AMU: count-based, mass-based, daily dose-based and course-based, each with its own advantages and disadvantages.

Results: The Netherlands, Belgium, Denmark and Switzerland use daily dose-based metrics to benchmark AMU at farm-level, but each country diverges from ESVAC methodology in its own way, including how the population 'at risk' is calculated. Germany operates a count-based system. Threshold AMU values have been specified at farm-level in the Netherlands, Belgium and Denmark, and action is required from producers to reduce AMU above these values. The Netherlands and Belgium also benchmark veterinarians.

Conclusions: For mixed species farms common in the UK and Ireland, splitting AMU by species is recommended. It is also recommended that HP-CIAs are benchmarked separately to other antimicrobials. No one metric is optimum; however, for ruminant livestock a daily dose-

based metric allows for country specific adaptations which may allow a higher degree of precision at farm-level benchmarking in the UK and Ireland.

INTRODUCTION

Globally, the use of antibiotics in farm livestock is attracting interest and concern in the wake of growing antimicrobial resistance (AMR) and fears of subsequent repercussions on human health[1,2]. Measurement of AMU is vital. ‘If you can’t measure something, you can’t understand it. If you can’t understand it, you can’t control it. If you can’t control it, you can’t improve it.’ (H. James Harrington). Benchmarking AMU at country-level, prescribing veterinarian-level or farm-level can highlight over-use, moves to particular antimicrobial groups and forms a basis for informed herd health discussions between farmers and veterinarians[3,4]. Benchmarking AMU also enables comparisons to be made between countries, vets, or farms. To do this effectively, a standardised metric is required when recording AMU. In 2017, several European health organizations (ECDC, EFSA and EMA) jointly established a list of indicators to measure AMU at national level[5]. Sales data was proposed to measure the overall effect of policy interventions and management measures. Such data are collected by most European countries, but as they are based on sales data from pharmaceutical companies or wholesalers they do not cater for farm-level benchmarking[6]. Numerous other systems have been developed to measure veterinary AMU using different metrics to express use. This review reports on the implementation of mandatory systems currently in use within Europe and makes recommendations for farm-level benchmarking of the ruminant livestock industry within the UK and Ireland.

TYPES OF METRICS

Metrics can be divided into count-based, mass-based, daily dose-based and course-base metrics (Table 1). Count-based metrics are the simplest to calculate and understand. An example of a count-based metric is dividing actual treatment days by potential treatment days taking into account the number of animals on farm. For the other three metrics, the quantity of AMU is either expressed directly as the mass of the active substance (mass-based), or the mass is adjusted based on the daily dose rate for the specific type of antimicrobial (dose-based) or for the daily dose rate for the type of antimicrobial and the course length (course-based). The adjustment is made by dividing the mass by the defined daily dose (DDD) which is the assumed 'average maintenance dose per day per kg body weight for the main indication in a specified species'[7], or defined course dose (DCD) which incorporates treatment duration[7]. The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) developed standardised DDD and DCD values based on the recommended dosage in nine EU countries[6], and these are developed for benchmarking at national level. The resulting figure is then divided by standard estimated mass of animals.. This mass is generally estimated by multiplying animal numbers (e.g. average number of animals or number of slaughter animals within a particular category) with assumed standard weights for the species category. ESVAC has established standard animal categories and weights based on the average weight at the time of treatment. These are used for the calculation of European statistics at national level[8], but countries tend to diverge from these standard weights to allow a more detailed categorization for their own statistics at farm level[9,10,11]. Both the way that the quantity of active substance is expressed and the way that the mass at risk is estimated can have consequences for practical data collection and for the quality of the resulting benchmark.

BENCHMARKING SYSTEMS IN PRACTICE THROUGHOUT EUROPE

European countries collect AMU sales data on a national level, allowing assessment of changes in national use over time and comparisons between countries[6]. Mandatory nation-wide benchmarking of farms is currently underway in five European countries as will be described, but only for certain species. Other countries have initiatives to reduce antimicrobial usage, voluntary benchmarking systems, or mandatory benchmarking under certain quality labels. These are beyond the scope of this paper but details can be found on the AACTING website (the network on quantification of veterinary Antimicrobial usage at herd level and Analysis, CommunicaTion and benchmarkING to improve responsible usage)[12].

Count-based (Germany)

One country in Europe currently uses a count-based metric. Since 2014 German pig, veal, beef, broiler and turkey farms are required to report their AMU to a central government-owned database (HIT)[13] along with number of treated animals, number of treatment days and the antimicrobial product used. Both veterinarians and farmers can report AMU. The farmer also reports the number of animals on the farm twice yearly which is used to calculate the number of animal days at risk. Reporting can be done via an online system, in writing, predefined spreadsheets, or automatic export from some farm management systems. Farms are compared to national benchmark values for each species and production group (cattle and pigs are each divided into two age categories). The median value and the upper quartile are calculated and used to categorise farms. The farmer receives bi-annual values and is obliged to compare their results with the national values[13]. A quality system covering about 95% of German broiler, veal, and pork production (Qualität und Sicherheit GmbH) also provides farmers with quarterly benchmarking reports using a count-based metric[14].

Daily dose-based (The Netherlands, Belgium, Denmark and Switzerland)

Four countries in Europe use DDD-based metrics to report on AMU. A synopsis of species benchmarked, how data is submitted and how often reports are issued is presented in Table 2. In the Netherlands and Denmark, AMU data is based on sales to the farm as only veterinarians are permitted to administer antimicrobials in The Netherlands (with a few exceptions)[15] and Danish vets are only permitted to prescribe antibiotics for a maximum of 5 days[16]. Therefore, the difference between sales and usage is not likely to differ considerably. In all four countries both the farmer and the veterinarian have to approve AMU data before it is submitted. In the Netherlands and Belgium, veterinarians are also benchmarked using a DDD-based metric[10,17].

Estimation of total mass at risk at farm-level is calculated differently in each country. The Netherlands diverges from ESVAC by using the average number of live animals throughout the year rather than slaughter data[9,10,18]. Furthermore, The Netherlands uses more detailed subdivisions of estimated bodyweights, and the actual weight of broilers and turkeys at treatment (rather than standard weight) as this data is readily available. Belgium uses country specific weights for veal and laying hens and the ESVAC weights for other species[11]. Denmark also uses country specific weights for benchmarking[19] and in Switzerland veterinarians are able to adapt the standard body weights for animals on an individual farm basis, if necessary[20].

In addition to diverging in the way animal mass at risk is calculated, countries also diverge from DDD as established by ESVAC by using country-specific recommended daily doses. In particular, the Netherlands and Belgium have made specific changes to allow more accurate monitoring. For example, Belgium uses a country specific metric (BD100) which uses country-specific recommended doses (DDDbel) based on an average for all indications with separate values for veal and other cattle[11]. Furthermore, special formulas were created to include products like topical sprays which have no value in the ESVAC methodology. BD100 also accounts for long acting antimicrobials in a different way to ESVAC, using the following equation expressed per 100 days (as opposed to ESVAC which uses a yearly value):

$$BD100 = \frac{mg\ active\ substance/DDDbel}{Total\ animal\ mass\ (kg) * period} * Long\ Acting\ factor * 100$$

The ‘long acting factor’ reflects that some products are only applied once, but remain active for a long period. It is the number of days after which repetition of the treatment is advised in the standard product documentation. For most products it is 1, and even for some long acting products (e.g., dry cow therapy and intra-uterine products) a value of 1 is used because using a higher value would lead to very high BD100 values and because their exact duration of antimicrobial action is unknown[17].

Countries that have established benchmarking for farms and veterinarians are able to set targets for AMU and consequences for producers or veterinarians with high AMU. The Netherlands have established ‘Signaling Values’ and ‘Action Values’ for each production type. A farm above the Signaling Value receives a warning, and those above the Action Value are legally required to take action. Originally the Action Value was set at the 75th percentile (i.e., the 25% of farms with the highest values were required to take action). These values are not stationary and therefore drive a continual decrease in veterinary AMU. No numerical Action Value is set anymore for cattle, instead, farms being above the Signaling Value for 2 years in a row are required to take action[10]. Belgium uses two threshold values set at the 50th and 90th percentile. Farms exceeding the 50th percentile are stimulated to make changes, with required changes being quicker and more extensive for farms exceeding the 90th percentile[11].

The Danish Veterinary and Food Administration (DVFA) use the ‘Yellow Card initiative’ to reduce AMU (in cattle and pigs). Separate AMU threshold values have been set for age and weight ranges in cattle and pigs. There are also weighting factors to emphasize the use of high priority critically important antimicrobials (HP-CIAs) which are used for human treatment. To discourage use, these HP-CIAs receive a weight of 10, whilst most other categories have a weight close to 1[21,22]. If a farm’s benchmark exceeds the threshold value a Yellow Card is issued and measures put in place. If this fails to reduce AMU to sub-threshold values a Red

Card is issued and the DVFA may compel the farmer to reduce AMU. The farmer has to pay a fee each time the threshold is not met and pays for all inspections and expert advice.

In the Netherlands, enforcement and development of measures to reduce AMU on-farm are primarily a task of certification bodies, and Belgium is likely to follow a similar pattern[15,17]. However, the government is responsible to enforce corrective changes within the veterinarian sector[17]. In Denmark, measures are established and enforced by the government[21].

IMPACT OF BENCHMARKING

Implementing mandatory farm-level AMU benchmarking enables a country to make comparisons between farms, thus identifying areas where the greatest reduction is needed. Denmark and the Netherlands have been benchmarking since 2010, the longest in Europe, and have considerably reduced AMU. After establishing the Yellow Card initiative, Denmark had a 10% decrease in veterinary AMU within 4 years and new targets have subsequently been set[21]. Veterinary AMU has reduced by 63% since benchmarking started in the Netherlands as measured by $DDDA_{F,}$ (Dutch farm benchmarking metric). Use of selective dry cow therapy led to a considerable drop in AMU in the Dutch dairy sector. However, reduction has been most difficult in the calf sector in which most farms have a value above the Signaling Value[10]. While these reductions in AMU are not solely due to benchmarking, it is an example of how measuring AMU can lead to its control and reduction.

DISCUSSION

Mass-based, dose-based and course-based metrics are corrected for the ‘mass of animals at risk’. Exact figures for the total animal mass are generally lacking, and there is debate on how it should be estimated. Standard weights established by ESVAC are used for the calculation of European statistics for benchmarking at the national level. However, ESVAC was not designed for farm level benchmarking for example, it mainly uses slaughter data, not the actual number of animals on farm, which provides an unfair advantage to farms selling a greater percentage of their animals for slaughter, rather than selling on to another farm[23]. Therefore, countries tend to diverge from these standard weights which allows more detailed and accurate categorization for their own statistics. Inaccurate estimates may provide unfair advantages to specific types of farms, and becomes especially problematic when comparing farms that diverge from the standardised weights. For example, farms with heavier than estimated animals would receive a higher AMU value than those with lighter animals despite applying the same level and number of treatments. This divergence from standard weights could be because of differences in the age at which animals leave the farm, or because they stock different breeds. ESVAC methodology.

It has been suggested that an accurate way of estimating the total weight is to integrate animal numbers and ages from national movement databases that record births, deaths and movements between farms[24]. In the case of designing an AMU system for ruminant livestock, these databases already exist for cattle in Great Britain (Cattle Tracing System), Northern Ireland (Animal and Public Health Information System) and Ireland (Animal Identification and Movement System). Cattle breed information is also available; therefore, it would be theoretically possible to calculate weight estimates using breed-specific growth curves. This could enable a highly accurate estimate of the total weight on farm without the need for additional data collection (as the information is already collected for cattle as a legal requirement). Breed and age data is currently lacking for sheep and goats; however, there is a movement towards an online system, currently available in England (ARAMS). Numbers of ewes on farm are available from census data and AMU could be presented on a ewe basis, not the slaughter lamb generation, as ewes are likely to receive more antimicrobials (mg/kg) than lambs. Due to the difference in the data available for benchmarking, metrics for cattle and sheep are likely to be designed separately. It is also likely that dairy cows and beef cows will be treated separately with metrics designed specifically for each enterprise.

It is important to emphasise that the choice between mass-based and DDD-based or DCD-based metrics can impact greatly on the figures obtained and the consequent influence on AMU policies[4,24,25]. For example, a mass-based metric applied to the UK dairy industry was heavily influenced by parenteral therapy, but poorly reflected the use of intra-mammary treatments. Whereas if a DDD-based metric was applied to the same data, it was heavily influenced by intra-mammary treatment of lactating cows but did not represent footbath usage[24]. Such differences could incentivise reductions in specific treatment routes, rather than an actual reduction in antibiotics overall. Different metrics also give a different impression of the proportion of HP-CIAs. If expressed as a mass-based metric, 5% of the antimicrobials used on UK dairy farms were HP-CIAs. However, if expressed as DDD-based metric the figure was 15-18%[24]. Taking into account the type of antimicrobial used is essential to avoid incentivising the use of antibiotics critical to human health[4,23]. Reduction of HP-CIAs specifically is a main aim of many national reduction programs; therefore, suggestions have been made to set separate calculations and targets for HP-CIAs as is done in the UK VARSS reports.

Mass-based metrics can simply rely on sales records for each type of antimicrobial (total antimicrobials sold to the farm). In contrast, for DDD-based- and DCD-based metrics it is also necessary to register the species. In practical terms this means that each time an antimicrobial is used the type, species and quantity needs to be recorded for DDD and DCD-based metrics. If multi-species farms are compared to each other using a mass-based metric without differentiating between species, the benchmark of these farms would depend on the species ratio. Recent studies in the UK using convenience samples, suggest a mean AMU on sheep farms was 11 mg/population corrected unit (PCU)[26], compared to 21 mg/PCU on dairy farms[24] and 19 mg/PCU on beef farms[27]. Therefore, AMU would likely be higher for farms which stock a smaller proportion of sheep and a larger proportion of cattle. Thus, separate recording for each species is preferable even under a mass-based metric, which removes the advantage of simplicity.

An advantage of mass-based metrics over DDD and DCD metrics is that these do not depend on assumptions about the dosage. Recommended doses may not always reflect drug use in practice due to large variations for dosage recommendations between products and countries for the same active substance[4,6]. On the other hand, to improve the accuracy of DDD- or DCD-based metrics, country-specific recommended doses have been developed in various countries. If a comparison between countries is desired, recalculation using the ESVAC standard dosages is possible without any further data collection. DDD- or DCD-based metrics also allow countries to set specific recommended doses for products that currently lack an ESVAC specified dose, e.g., intramammary tubes for dry cows, topical sprays and footbaths[24,25]. However, if DDD-based and DCD-based metrics become too specific (e.g. assigning doses to specific ages or breeds) this can become a disadvantage as this data is more difficult to collect. In Denmark, this specificity has been problematic at times; therefore, drugs administered by the veterinarian were usually excluded from analyses because precise information on the animal species, age-group, or indication was lacking[28]. However, as farmers in the UK and Ireland are currently able to store and administer antibiotics on farm, involving farmers in the creation of benchmarking systems may incentivise them to record AMU accurately.

As neither mass-based, DDD-based nor DCD-based metrics will fulfil all requirements when benchmarking AMU on farm level[29] simultaneous use of multiple metrics has been suggested[24]. Multi-metrics may be confusing to producers and could lead to the most favorable report being presented, or results not being compared like-for-like. Therefore, one standard metric per species may be beneficial for farm-level benchmarking. As established previously, it will be beneficial to split AMU by species and also to benchmark HP-CIAs separately; therefore, the data collected under even the simplest count- or mass-based metric on multi-species farms common in the UK and Ireland should include species and type of antimicrobial. As this removes the simplicity of these metrics, it could be beneficial to complete the final step and adjust the antimicrobials for potency, enabling DDD-based and DCD-based metrics to be used. Both DDD and DCD-based metrics allow for country specific dosages to be set in line with the practices common within the country. The precision of DDD and DCD-based metrics could be improved if used in conjunction with online animal record databases, such as are available in the UK and Ireland for cattle. Therefore, if a single metric was used per species, DDD-based or DCD-based metrics may be the most promising in terms of collecting data that is a true reflection of on-farm AMU.

CONCLUSION

There is no consensus for the 'optimum' metric for capturing AMU on a farm or country level. The way that the amount of antimicrobials used is expressed and the estimation of the population 'at risk' will affect the outcome of a benchmarking system. For mixed species farms common in the UK and Ireland, splitting antimicrobials by receiving species is advisable within any benchmarking system. Daily dose- or course-based metrics can provide an accurate reflection of AMU in cattle by using the cattle movement databases already in place. If the UK wishes to create UK-specific defined doses and courses, a DDD or DCD-based metric could enable a highly-specific benchmarking system. It is also recommended that HP-CIAs are presented and benchmarked separately from other antibiotics to avoid incentivising their use. The UK and Ireland will benefit from an industry-wide benchmarking incentive to reduce AMU in ruminant livestock as has been done in several European countries.

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Table 1. Overview of four types of metrics of AMU

Type of metric	Example equation
Count-based	$\frac{Number\ of\ \ animals\ treated * treatment\ days\ per\ animal}{Total\ number\ of\ animals * total\ number\ of\ days}$
Mass-based	$\frac{Total\ quantity\ of\ active\ substance\ used\ (mg)}{Estimated\ total\ animal\ mass\ at\ risk\ (kg)}$
Dose-based	$\frac{Total\ quantity\ of\ active\ substance\ used\ (mg)\ /\ DDD\ (mg/kg)\ \dagger}{Estimated\ total\ animal\ mass\ at\ risk\ (kg)}$
Course-based	$\frac{Total\ quantity\ of\ active\ substance\ used\ (mg)/\ DCD\ (mg/kg)\ \ddagger}{Estimated\ total\ animal\ mass\ at\ risk\ (kg)}$

**Note that some authors seem to use the abbreviation DDD or DCD to indicate this entire equation, but this diverges from the original definitions by EMA (2015) which we will use in this article.*

† DDD; Defined Daily Dose. As per ESVAC, intramammaries (lactating cow) expressed at tubes/animal rather than mg/kg

‡ DCD; Defined Course Dose, intramammaries (lactating and dry cow) expressed at tubes/animal rather than mg/kg

Table 2: Overview of daily dose-based metrics in Europe

Country	Species Benchmarked (year)	AMU submission	Reports Issued:
The Netherlands[7,8]	Veal (2010) Broiler (2010) Pig (2010) Cattle (2012) Turkeys (2013) Laying Hens (2018) Rabbits (2018)	Veterinary practice software Online database	Annually (Government reports) Quarterly (Producer Reports)
Belgium[9]	Veal (2017) Broiler (2017) Laying Hens (2017) Pigs (2017) Cattle (Optional)	Online Database Standardised Excel sheet Veterinary practice software	Quarterly
Denmark[15]	Cattle (2010) Pigs (2010)	Online database Invoice or registration of sales from: Vets, Pharmacies or Feed mills	9 month periods
Switzerland[16]	TBC (2020)*	Veterinary practice software Online database App	TBC

**Switzerland collect AMU data on all species, including pets, but benchmarking has not commenced and benchmarking may not include all species.*